REMARKS

Claims 1 to 12 are pending in the application.

Claims 1, 7, 8, 10, and 12 are currently amended.

Claims 2, 4 to 6, 9, and 11 are original.

Claim 3 is canceled.

Claims 1, 2, and 4 to 12 would be all of the pending claims if the present amendment is entered.

Discussion Of Claim Amendments

Claims 1 and 8 are amended to delete subject matter that is not part of the elected invention of Group II, and Claim 3 is canceled for being drawn to a non-elected invention. Claim 1 is further amended to restrict the definition of the group "Q" to the definitions of original claims 4 and 5, which depend from claim 1. Claim 7 is amended to change its dependencies, as claim 3 is canceled. Claims 10 and 12 are amended to place the claims in proper form in accordance with MPEP §608.01(n)(I)(B)(3) by literally reciting what was previously incorporated by reference from claim 8.

Election/Restrictions

Applicants had elected in their previous paper Group II, Claims 1, 2, and 4 to 12 in part, drawn to a naphthyridine compound (i.e., Y is C(=O), CH_2, or $C(H)(R^7)$, W^1 is $C(H)R^5$ or CR^5, one of W^2, W^3, and W^4 is N and the other two of W^2, W^3, and W^4 are CR^5, classified in class 546, subclass 122, the composition, and method of uses thereof. Applicants thank the Examiner for correcting the description of Group II.

As requested, Applicants have currently amended the claims to conform to the subject matter of Group II.

Claim Rejections - 35 U.S.C. § 102

Claims 1, 2, 4, and 9 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hadley et al. (U.S. 6,245,778). In the Office Action, it was alleged that the

compounds of claim 2 (columns 22-23), and the pharmaceutical compositions thereof, of Hadley et al. are encompassed by the instant claims wherein "Q is $NR^6C(O)$," R^1 is substituted phenyl, Y is CH_2, and R^2 is alkyl.

Applicants respectfully traverse the rejection because the compounds of Hadley et al. contain the group C(O)-N(H), whereas the Q group that was identified in the Office Action has the reverse orientation, namely $N(R^6)C(O)$. Accordingly, the compounds and pharmaceutical compositions of Hadley et al. do not anticipate the compounds of claim 1, 2, 4, or 9, and thus these claims are patentable under 35 U.S.C. § 102(b) in view of Hadley et al.

Claims 1, 2, and 9 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ohno et al. (U.S. 5,367,078). It was alleged in the Office Action that the compounds of examples 58-61 and 63-78 in Table 4 (columns 33-36), and the pharmaceutical compositions thereof, of Ohno et al. are encompassed by the instant claims wherein R^1 is optionally substituted phenyl or heteroaryl, R^3 is OH, which may tautomerized to oxo, Q is oxadiazol-2,4-diyl, Y is CH_2, and R^2 is phenylalkyl.

Applicants respectfully traverse the rejection because claim 1 is amended to incorporate the limitations of original claims 4 and 5, wherein Q is $N(R^6)C(O)$ or Q is $C{=}C$, $CH_2C{\equiv}C$, $C{\equiv}CCH_2$, $CF_2C{\equiv}C$, or $C{\equiv}CCF_2$, respectively. Accordingly, the compounds and pharmaceutical compositions of Ohno et al. do not anticipate the compounds of claims 1, 2, or 9, and thus these claims are patentable under 35 U.S.C. § 102(b) in view of Ohno et al.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 1, 2, 4 to 7, 9, and 11 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for making and using the compound of claim 8, allegedly does not reasonably provide enablement for the compounds wherein two adjacent, substantially sp^2 carbon atoms together comprise a ring. Particularly, it was alleged in the Office Action that the specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without undue experimentation. Invention compounds having two adjacent, substantially sp^2 carbon atoms together comprise a ring, and starting material and process for making such compounds, allegedly have not been specifically described or enabled. It was further argued that not all of the claimed invention compounds, especially the compounds having two adjacent, substantially sp^2 carbon atoms together comprise a ring, are effective matrix metalloproteinase inhibitors and are useful for the treatment of osteoarthritis or rheumatoid arthritis.

Applicants respectfully traverse the rejection because they believe that the skilled artisan would have been able to practice the invention of claims 1, 2, 4 to 7, 9, and 11 without undue experimentation for the reasons provided below.

"The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue" (MPEP 2164.01 under the heading UNDUE EXPERIMENTATION). Further, the experimentation can be complex but not undue, because the art typically engages in such experimentation (MPEP 2164.01 under the heading UNDUE EXPERIMENTATION). Still further, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (citing *In re Angstadt*, 537 F.2d 489, 502-504, 190 USPQ 214, 218 (CCPA 1976).

The invention compounds having two adjacent, substantially sp^2 carbon atoms together comprise a ring relate to substituents described for substituted R^1 and R^2 groups in the compound of Formula I of claim 1. Claims 2, 4 to 7, 9, and 11 incorporate the limitations of claim 1, and thus Applicants remarks regarding claim 1 also apply to claims 2, 4 to 7, 9, and 11.

In claim 1, substituted R^1 groups include:

Substituted C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted phenyl;

Substituted naphthyl;

Substituted 5- or 6-membered heteroaryl; and

Substituted 8- to 10-membered heterobiaryl;

and substituted R^2 groups include:

Substituted phenyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

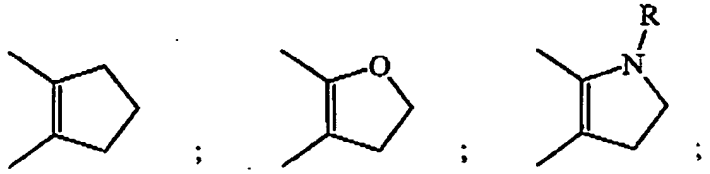
Substituted phenyl-O-(C_1-C_8 alkylenyl);

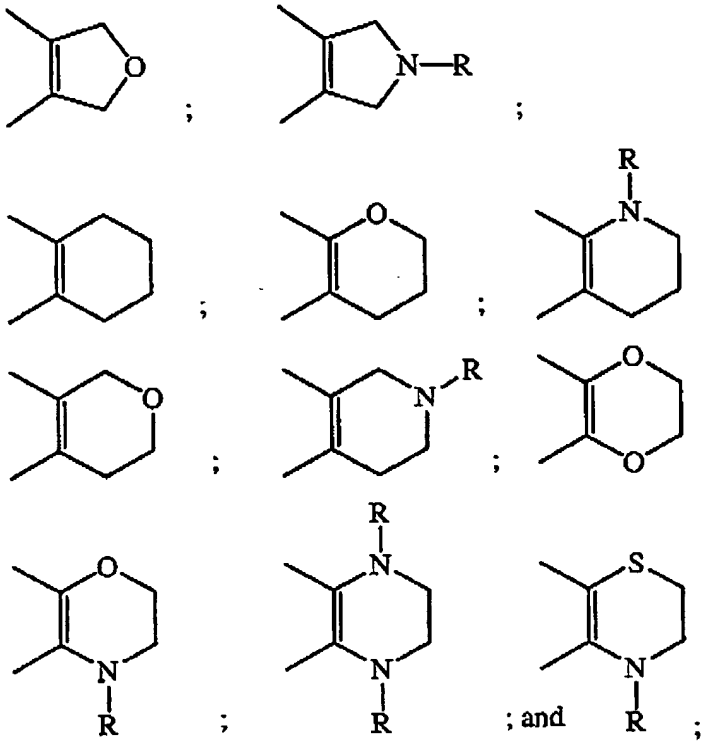
Substituted phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl).

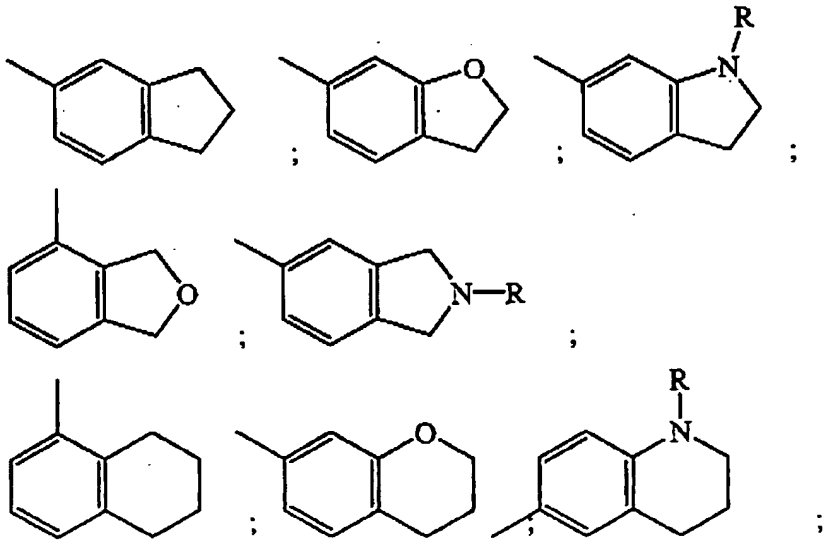
As described in claim 1, each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom. The substituents include, *inter alia*, two adjacent, substantially sp^2 carbon atoms taken together with a diradical substituent to form a cyclic diradical selected from:

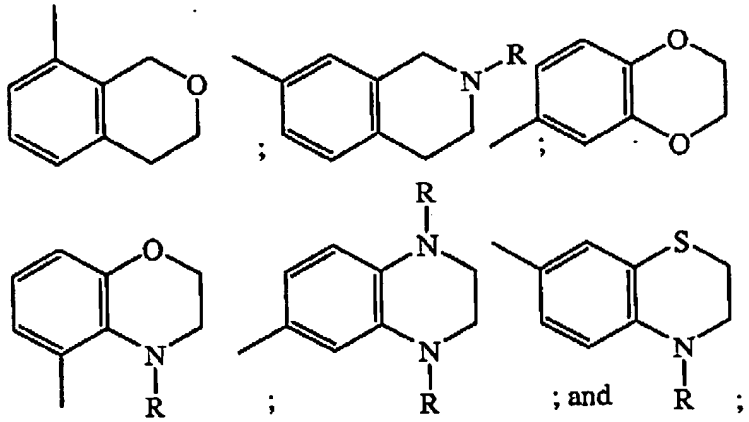




wherein R is H or C_1-C_6 alkyl.

For illustration, such a substituted phenyl wherein two adjacent, substantially sp^2 carbon atoms are taken together to form a cyclic diradical substituent includes the following radical groups for R^1 and R^2:





wherein R is as defined above.

Starting materials such as bromo-indoles, bromo-indanes, and bromo-3,4-methylenedioxy)benzene were commercially available at the time the application was filed or could have been readily prepared by the skilled artisan using routine methods. The specification on page 94, at line 3, to page 96, at line 18, teaches how to functionalize such R^1 and R^2 groups in order to prepare a compound of Formula I. These R^1 and R^2 groups may be coupled, if necessary, to a compound of Formula I such as the naphthyridines of formulas (F), (G), and (H) in Figure 2 on pages 77-78 of the specification. Accordingly, Applicants believed that the skilled artisan would have been able to routinely prepare the compounds of Formula I in claim 1 at the time of filing the present application without undue experimentation in view of the guidance provided in the specification.

Further, the specification on page 52, at line 15, to page 53, at line 15, provides guidance to the skilled artisan about the binding of compounds of claim 1 to MMP-13. This guidance teaches the skilled artisan that the R^1 and R^2 groups of the Formula I would be tolerated without drastically altering biological activity due to the opening to the substrate groove at the top of the "sock" and the discovery of the S1" binding pocket, which is open to solvent. Accordingly, Applicants believe that at the time of filing the present application the skilled artisan would have been able to use the compounds of

Formula I in claim 1 to inhibit MMP-13 and treat osteoarthritis or rheumatoid arthritis without undue experimentation in view of the guidance provided in the specification.

In view of the above remarks, Applicants believe that claims 1, 2, 4 to 7, 9, and 11 are enabled, and are thus patentable under 35 U.S.C. § 112, first paragraph.

Allowable Subject Matter

Claims 8, 10, and 12 are objected to as allegedly being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicants respectfully traverse the objection in view of the above amendments and remarks, which Applicants believe have overcome the rejections of base claim 1.

Conclusion

In view of the above amendments and remarks, Applicants believe that the rejections and objection are overcome and request reconsideration of claims 1, 2, and 4 to 12.

Respectfully submitted,

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